

Application No. 10/601171

Attorney Docket No. SYNI-003CN

Application No. 10/601171

1-60 (Canceled)

61. (Currently Amended) A composition comprising an amount of a monoclonal antibody effective to treat neonates having a staphylococcal infection and a pharmaceutically acceptable carrier, wherein the antibody having binding specificity specifically binds to poly-glycerol phosphate of Lipoteichoic acid (LTA) of Gram positive bacteria with a binding affinity of about 10<sup>-8</sup> M or higher and is of the IgG isotype and a, wherein the antibody i) binds to both coagulase positive and coagulase negative Staphylococci, ii) and enhances opsonization of Gram positive bacteria multiple serotypes of *Staphylococcus epidermidis*, coagulase negative staphylococci and *Staphylococcus aureus* by phagocytic cells over background with or without complement as compared to an appropriate control in an in vitro opsonization assay, and iii) confers a statistically significant enhancement of survival or reduces bacteremia in an animal model, wherein the composition is formulated for pharmaceutical administration

62. (Previously Presented) The composition of claim 61, wherein the opsonization assay is performed in the presence of complement, phagocytic cells, or both.

63. (Previously Presented) The composition of claim 62, wherein the complement or cells or both are human in origin

64. (Canceled)

65. (Previously Presented) The composition of claim 62, wherein the phagocytic cells comprise macrophages, monocytes, neutrophils, or combinations thereof

66. (Previously Presented) The composition of claim 62, wherein opsonization is measured by determining opsonophagocytic bactericidal activity.

Application No. 10/601171

Attorney Docket No. SYN1-003CN

67. (Previously Presented) The composition of claim 61, wherein the antibody is capable of binding to LTA of Gram positive bacteria fixed to a solid support.

68. (Previously Presented) The composition of claim 67, wherein the solid support is a plate well, bead, or micro-bead.

69. (Canceled)

70-76. (Canceled)

77. (Currently Amended) A composition comprising a monoclonal antibody which specifically binds to poly-glycerol phosphate of LTA of Gram positive bacteria with a binding affinity of 10<sup>-8</sup> M or higher, or antigen binding fragment thereof, and a pharmaceutically acceptable carrier, wherein the monoclonal antibody has binding specificity to LTA comprises, wherein at least one heavy chain variable region or light chain variable region of the antibody has at least 70% amino acid identity with at least one heavy or light chain variable region of the monoclonal antibody 96-110 MAB and a carrier the complementarity determining regions (CDRs) of the heavy and light chain variable regions of monoclonal antibody 96-110 set forth as SEQ ID NO:87 and SEQ ID NO:89.

78. (Canceled)

79. (Previously Presented) The composition of claim 61 or 77, wherein the antibody comprises a portion of a human antibody sequence.

80 (Previously Presented) The composition of claim 79, wherein the portion of human antibody sequence comprises an Fc region.

81. (Previously Presented) The composition of claim 61 or 77, wherein the antibody specifically binds LTA exposed on the surface of the cell wall of Gram positive bacteria.

Application No. 10/601171

Attorney Docket No. SYNI-003CN

## 82-85. (Canceled)

86. (Previously Presented) The composition of claim 85, wherein the antibody binds to serotype 5, serotype 8, or both serotype 5 and serotype 8 of *Staphylococcus aureus*.

87. (Currently Amended) The composition of claim 61 or 77, wherein the antibody additionally specifically binds to LTA of *Staphylococcus epidermidis* and one or more Gram positive bacteria selected from the group consisting of *Staphylococcus aureus*, *Streptococcus mutans*, *Streptococcus faecalis*, and *Streptococcus pyogenes*.

## 88-90. (Canceled)

91. (Previously Presented) The composition of claim 61 or 77, wherein the antibody reduces LTA-mediated inflammation, LTA-mediated cytokine production, or combination thereof.

## 92. (Canceled)

93. (Previously Presented) The composition of claim 77, wherein the antibody is an Fab, Fab', F(ab')2, or sFv fragment of an antibody.

94. (Previously Presented) The composition of claim 61 or 77, further comprising at least one additional monoclonal antibody having specificity for LTA.

95 (Currently Amended) A pharmaceutical composition comprising an effective amount of an antibody of claim 61 or 77, for use in a human neonate.

96 (Withdrawn) A polynucleotide encoding an antibody, or fragment thereof, of claim 61, 77, or 88.

Application No. 10/601171

Attorney Docket No. SYNI-003CN

97. **(Withdrawn)** The polynucleotide of claim 96, wherein the polynucleotide encoding the variable region of the antibody, or fragment thereof, has at least 70% identity to the polynucleotide set forth in FIG. 12.

98. **(Withdrawn)** A vector comprising the polynucleotide of claim 96.

99. **(Withdrawn)** A cell comprising the polynucleotide of claim 96 or the vector of claim 98.

100. **(Withdrawn)** An antibody, or fragment thereof, produced by a cell comprising a polynucleotide or vector comprising a polypeptide encoding an antibody of claim 61 or 77.

101. **(Currently Amended)** The composition of claim 61, wherein the antibody is of the IgG IgG1 isotype.

102-103. **(Canceled)**

104. **(New)** A composition comprising a monoclonal antibody which specifically binds to poly-glycerol phosphate of LTA of Gram positive bacteria with a binding affinity of  $10^{-8}$  M or higher, or antigen binding fragment thereof, and a pharmaceutically acceptable carrier, wherein the monoclonal antibody comprises the heavy chain variable region set forth as SEQ ID NO.87.

105. **(New)** A composition comprising a monoclonal antibody which specifically binds to poly-glycerol phosphate of LTA of Gram positive bacteria with a binding affinity of  $10^{-8}$  M or higher, or antigen binding fragment thereof, and a pharmaceutically acceptable carrier, wherein the monoclonal antibody comprises the light chain variable region set forth as SEQ ID NO.89.

106. **(New)** A composition comprising a monoclonal antibody which specifically binds to poly-glycerol phosphate of LTA of Gram positive bacteria with a binding affinity of  $10^{-8}$  M or higher, or antigen binding fragment thereof, and a pharmaceutically acceptable carrier, wherein the monoclonal antibody comprises a heavy chain comprising the heavy chain complementarity

Application No. 10/601171

Attorney Docket No. SYNI-003CN

determining regions (CDRs) of the monoclonal antibody 96-110 and a variable region having 80% amino acid identity with SEQ ID NO:87.

107. (New) The composition of claim 106, wherein the variable region has 85% amino acid identity with SEQ ID NO:87

108. (New) The composition of claim 106, wherein the variable region has 90% amino acid identity with SEQ ID NO:87.

109. (New) The composition of claim 106, wherein the variable region has 95% amino acid identity with SEQ ID NO:87.

110. (New) A composition comprising a monoclonal antibody which specifically binds to poly-glycerol phosphate of LTA of Gram positive bacteria with a binding affinity of  $10^{-8}$  M or higher, or antigen binding fragment thereof, and a pharmaceutically acceptable carrier, wherein the monoclonal antibody comprises a light chain comprising the light chain complementarity determining regions (CDRs) of the monoclonal antibody 96-110 and a variable region having 80% amino acid identity with SEQ ID NO:89

111. (New) The composition of claim 110, wherein the variable region has 85% amino acid identity with SEQ ID NO:89.

112. (New) The composition of claim 110, wherein the variable region has 90% amino acid identity with SEQ ID NO:89.

113. (New) The composition of claim 110, wherein the variable region has 95% amino acid identity with SEQ ID NO:89.

114. (New) A composition comprising a monoclonal antibody and a pharmaceutically acceptable carrier, wherein the monoclonal antibody i) specifically binds to poly-glycerol phosphate of LTA of Gram positive bacteria with a binding affinity of  $10^{-8}$  M or higher, ii) binds

Application No. 10/601171

Attorney Docket No. SYNI-003CN

to and enhances opsonization of multiple serotypes of *Staphylococcus epidermidis*, coagulase negative staphylococci, and *Staphylococcus aureus* by phagocytic cells with or without complement as compared to an appropriate control in an in vitro opsonization assay, and iii) comprises a heavy chain comprising the complementarity determining regions (CDRs) of the monoclonal antibody 96-110 heavy chain variable region set forth as SEQ ID NO:87 and having at least 70% amino acid identity with the monoclonal antibody 96-110 heavy chain variable region set forth as SEQ ID NO:37.

115. (New) A composition comprising a monoclonal antibody and a pharmaceutically acceptable carrier, wherein the monoclonal antibody i) specifically binds to poly-glycerol phosphate of LTA of Gram positive bacteria with a binding affinity of  $10^8$  M or higher, ii) binds to and enhances opsonization of multiple serotypes of *Staphylococcus epidermidis*, coagulase negative staphylococci, and *Staphylococcus aureus* by phagocytic cells with or without complement as compared to an appropriate control in an in vitro opsonization assay, and iii) comprises a light chain comprising the complementarity determining regions (CDRs) of the monoclonal antibody 96-110 light chain variable region set forth as SEQ ID NO:89 and having at least 70% amino acid identity with the monoclonal antibody 96-110 light chain variable region set forth as SEQ ID NO:89.